Out-of-Hospital Cardiac Arrest in Men and Women
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Background—The incidence of sudden cardiac death is roughly 3 times greater in men than in women. However, in patients treated for out-of-hospital cardiac arrest, the relationships between sex and survival after adjustment for age and cardiac rhythm are unclear.

Methods and Results—In this retrospective cohort study, we examined 7069 men and 2582 women who were treated for out-of-hospital cardiac arrest in Seattle and suburban King County between 1990 and 1998. We compared successful prehospital resuscitation (hospital admission) and survival from event to discharge in men and women. Women had markedly reduced rates of ventricular fibrillation (VF), slightly older age, fewer witnessed arrests, and fewer arrests in public locations than men. Although their unadjusted resuscitation rate was lower (29% versus 32%, P<0.0001), women had a greater likelihood of resuscitation than men after adjustment for VF (odds ratio [OR] 1.13; 95% confidence interval [CI], 1.03 to 1.25) and after adjustment for VF plus additional factors (OR, 1.27; 95% CI, 1.14 to 1.41). The difference in resuscitation rates between men and women decreased as they aged (test for trend, P<0.0001). Unadjusted survival rates were also lower in women than in men (11% versus 15%, P<0.0001). Women had similar survival after adjustment for VF (OR, 0.97; 95% CI, 0.85 to 1.11) and after adjustment for VF plus additional factors (OR, 1.09; 95% CI, 0.93 to 1.27).

Conclusions—The lower unadjusted resuscitation and survival rates observed in women were primarily due to women’s lower incidence of VF, a relatively favorable cardiac rhythm. After adjustment for VF and other factors, women had higher resuscitation rates than men, but similar rates of survival from event to discharge. (Circulation. 2001;104:2699-2703.)

Key Words: women ■ heart arrest ■ fibrillation ■ sex

Sudden cardiac death is estimated to be the cause of 300,000 deaths in the United States annually and the cause of ≥50% of all cardiovascular deaths.1 Although women have less sudden cardiac death than men,2 survival differences between men and women after out-of-hospital cardiac arrest have not been closely examined. Studies examining out-of-hospital cardiac arrest have focused on emergency medical services (EMS) rather than on sex differences.3-6 Prior studies of out-of-hospital cardiac arrest that did compare men and women found that (1) women tended to have higher successful prehospital resuscitation rates than men, which led to higher hospital admission rates, but (2) women had equivalent or lower overall survival to hospital discharge rates than men.7-10

The reasons for the different outcomes between men and women are unclear. It is possible that women’s hormonal status influences their outcome, because younger women seem to have different outcomes than younger men in several studies. In an examination of the Scottish Monitoring Trends and Determinants of Cardiovascular Disease (MONICA) population, women <65 years of age had relatively lower cardiac case fatality rates than men outside the hospital, but women had relatively higher case fatality rates once admitted.11 In studies of acute coronary syndrome registries,12,13 young women had worse hospital mortality than young men, but older women and men had similar mortality rates. However, studies of out-of-hospital cardiac arrest did not or were not able to examine survival differences between men and women in different age groups after adjusting for multiple factors.

We now report on 2 large, long-standing, population-based databases of all out-of-hospital cardiac arrests for the City of Seattle and suburban King County, Washington. In these communities, patients with ventricular fibrillation (VF) treated for cardiac arrest have a survival rate of 25% to 30% and bystander cardiopulmonary resuscitation (CPR) rate >50%.4,10 In this study, we examined the differences between men and women who experienced out-of-hospital cardiac arrest. We compared (1) successful prehospital resuscitation (hospital admission) and (2) survival from event to hospital discharge.
Methods

Data Collection
In the city of Seattle, Washington, a prehospital emergency medical system, Medic I, has managed and established a surveillance system for all out-of-hospital resuscitation since March 1970. In adjacent King County, a similar surveillance system has also identified every case of out-of-hospital cardiac arrest receiving emergency care since 1974. In both systems, EMS treatment is provided by tiered response systems. Firefighters trained as emergency medical technicians constitute the first response and provide basic life support (BLS), ie, CPR and automated defibrillation for victims of cardiac arrest. Paramedics constitute the second response and provide advanced cardiac life support (ACLS), which consists of defibrillation, endotracheal intubation, placement of intravenous lines, and administration of medications.

The following data were abstracted from the existing databases: sex, age, whether collapse was witnessed, whether bystander CPR was performed, categorized location of arrest, response intervals of EMS units, first identified cardiac rhythms, hospital admission, and hospital survival. In Seattle, response intervals were calculated from dispatch of EMS and in King County, from call receipt to arrival of the vehicles at the scene. Accordingly, the King County response intervals were shortened by 1 minute, as estimated by the average measured time difference between call receipt and dispatch. In the Seattle case series, the first recorded cardiac arrest rhythm was determined by quality assurance staff, consisting of a nurse and clinical technician. An automated external defibrillator was applied to ~85% of the patients in cardiac arrest. For these cases, quality assurance staff reviewed the ECG strip from the first defibrillator analysis and recorded the rhythm from the strip. In the very few cases where the ECG strip was unavailable, the rhythm was recorded as VF if the defibrillator recommended a shock. If no shock was recommended, quality assurance staff used the rhythm that the paramedics noted on the medical incident report when they arrived as the first rhythm. This latter source was also used for the first rhythm for patients when the paramedics were the first responders on the scene. Cardiac cause of arrest was defined differently in the 2 databases; therefore, cause was not examined as a covariate. In Seattle, the identification of obvious noncardiac causes was determined solely from the EMS reports submitted by paramedics. In suburban King County, cause was determined from EMS reports and death certificates. Hospital discharge summaries and autopsy reports, when available, were also used.

Two outcome measures were available from the combined data sets. First, resuscitation was defined as hospital admission; patients were classified as (1) resuscitated and admitted to hospital or as (2) expired. Second, survival was measured from event to hospital discharge for all patients treated by EMS. In other words, the survival rate was based on all cardiac arrests seen by EMS, regardless of hospital admission. This retrospective database study was approved by the University of Washington Institutional Review Board.

Subjects
The study retrospectively examined patients ≥30 years of age who were treated for cardiac arrest between January 1, 1990, and December 31, 1998, in suburban King County and between January 1, 1990, and December 31, 1997, in Seattle, Washington. A cardiac arrest case was defined as a person who was unconscious and pulseless unrelated to trauma. The main analyses focused on cases treated by EMS (ie, received BLS or ACLS). A subanalysis examined differences between treated and untreated cases in Seattle.

Analysis
Comparisons between categorical and continuous variables were evaluated with χ² and t tests, respectively. We conducted unconditional logistic regression with prehospital resuscitation and survival as the outcomes, entered relevant covariates into the models, and calculated their interactions with sex. If the interaction terms were significant at P<0.05, they were included in the model. To confirm the results, we also performed stepwise logistic regression. After stratification for rhythm, covariates included in the model were age (by decade), location of arrest, witnessed arrest (yes or no), EMS response intervals, bystander CPR, and EMS-witnessed arrest. We specifically investigated whether an interaction existed between sex and age. Multivariate calculations excluded cases with unknown values for one or more covariates.

When we compared the baseline characteristics of men and women, we noted that the rate of VF was substantially lower in women. Therefore, in a post hoc analysis, we investigated whether this difference persisted after adjustment for other factors, such as witnessed arrest, location of arrest, and length of EMS response times. In another post hoc analysis, we examined if different rates of resuscitation in men and women were due to differences in the EMS treatment of cardiac arrest.

Results

Baseline Characteristics
From 1989 through 1997/1998, 7069 men and 3810 women aged ≥30 years experienced cardiac arrest unrelated to trauma and received BLS or ACLS in Seattle and suburban King County, Washington (combined 1990 population: 416 928 men and 447 462 women ≥30 years of age). In these cases, all of whom received EMS treatment, women had a lower annual rate of cardiac arrest than men (0.085% versus 0.16%, P<0.0001). Baseline demographic factors and unadjusted outcomes are listed in Tables 1 and 2. Compared with men, women had a much lower rate of VF. They were slightly older and slightly less likely to have a witnessed arrest or public location of collapse. In the Seattle database, women and men had similar rates of arrest due to a presumed cardiac cause (82% versus 81%, P=0.30) whereas in the King County database, men had arrest due to a presumed cardiac cause more often than women (73% versus 60%, P<0.0001).

Ventricular Fibrillation
Women with cardiac arrest were about half as likely as men to be found in VF (odds ratio, 0.51; 95% confidence interval [CI], 0.46 to 0.56, P<0.0001) even after adjustment for age, witnessed or unwitnessed arrest, public location of arrest, response intervals, and performance of CPR by bystanders or EMS. There were no interactions between sex and other factors; in particular, this finding did not vary significantly across age groups.

Successful Prehospital Resuscitation (Hospital Admission)
Overall, women had a lower unadjusted rate of resuscitation than men (Table 2). However, when we adjusted for the presence of VF, women had a greater odds of resuscitation (OR, 1.13; 95% CI, 1.03 to 1.25). Women in VF had a higher unadjusted resuscitation rate than men in VF, whereas women and men with pulseless electrical activity (PEA/asystole had similar unadjusted resuscitation rates (Table 2). Therefore, women’s lower rate of VF, a relatively favorable cardiac rhythm, was primarily responsible for their lower rate of resuscitation. In a multivariate model adjusting for VF and other significant factors (age, witnessed arrest, bystander...
CPR, categorized location of arrest, response time by first responder, and response time by paramedic) also showed women had greater odds of resuscitation than men (OR, 1.27; 95% CI, 1.14 to 1.41). Women in VF had higher adjusted odds of resuscitation than men in VF (OR, 1.44; 95% CI, 1.21 to 1.70), and women in PEA had higher adjusted odds of resuscitation than men in PEA (OR, 1.18; 95% CI, 1.02 to 1.36).

We observed a significant interaction between sex and age in VF patients, suggesting that the relation between sex and prehospital resuscitation was not constant across age groups. When we compared men and women stratified by age in decades, we observed a difference between younger women and younger men (Figure). Younger women in VF had a higher odds of resuscitation (hospital admission) than younger men in VF after adjustment for witnessed arrest, location of arrest, CPR, and response intervals. The difference between men and women progressively declined as women aged (test for trend, P<0.0001). Women and men >60 years of age had similar adjusted odds of resuscitation. The interaction between sex and age was not present in patients with PEA/asystole.

\section*{Survival From Event to Hospital Discharge}

The unadjusted overall survival rate in women was lower than that in men (Table 2). However, when we adjusted for the presence of VF, women had a similar odds of survival (OR, 0.97; 95% CI, 0.85 to 1.11). Women and men in VF had unadjusted similar survival rates (Table 2). Again, the unadjusted survival rates were similar for women and men in PEA/asystole (Table 2). Accordingly, women’s overall lower survival was related to their lower incidence of VF. A multivariate model, adjusted for VF and other factors (age, witnessed arrest, bystander CPR, categorized location of arrest, response time by first responder, and response time by paramedic) also showed women had odds of survival similar to those of men (OR, 1.09; 95% CI, 0.93 to 1.27). We found no significant interactions for survival between sex and other factors, including age.

\begin{table}[h]
\centering
\caption{Baseline Characteristics} \label{table1}
\begin{tabular}{lccr}
\hline
 & Men & Women & P \\
\hline
Presumed cardiac cause of arrest, n (%) & 5408 (77) & 2582 (68) & <0.0001 \\
Arrest in city of Seattle, n (%) & 2880 (41) & 1581 (41) & 0.45 \\
Age, y & 66 & 71 & <0.0001 \\
Witnessed status of arrest, n (%) & & & \\
Witnessed arrest & 3825 (54) & 1841 (48) & <0.0001 \\
Unwitnessed arrest & 2857 (40) & 1762 (46) & \\
Unknown & 387 (6) & 207 (5) & \\
Initial rhythm, n (%) & & & <0.0001 \\
VF & 3025 (43) & 939 (25) & \\
PEA/asystole & 3912 (55) & 2787 (73) & \\
Unknown & 132 (2) & 84 (2) & \\
Performance of CPR, n (%) & & & 0.25 \\
No bystander CPR & 3040 (43) & 1638 (43) & \\
Bystander CPR & 3332 (47) & 1709 (45) & \\
EMS CPR at time of arrest & 639 (9) & 432 (11) & \\
Unknown & 58 (1) & 31 (1) & \\
Location of arrest, n (%) & & & <0.0001 \\
Home & 4936 (70) & 2848 (75) & \\
Public location & 1625 (23) & 397 (10) & \\
Nursing home & 456 (6) & 524 (14) & \\
Other or unknown & 52 (1) & 41 (1) & \\
Response interval of first arriving unit, min & 4.4 & 4.4 & 0.81 \\
Response interval of paramedics, min & 9.3 & 9.4 & 0.51 \\
\hline
\end{tabular}
\textit{Values are mean or n (%).}
\end{table}

\begin{table}[h]
\centering
\caption{Successful Prehospital Resuscitation (Hospital Admission) and Survival From Event to Hospital Discharge} \label{table2}
\begin{tabular}{lccr}
\hline
 & Men & Women & P \\
\hline
Successful prehospital resuscitation (hospital admission) & 2282 (32) & 1094 (29) & <0.0001 \\
Patients with initial VF & 1522 (51) & 533 (57) & 0.001 \\
Patients with initial PEA/asystole & 728 (19) & 533 (19) & 0.57 \\
Survival from event to hospital discharge & 1056 (15) & 403 (11) & <0.0001 \\
Patients with initial VF & 843 (28) & 271 (29) & 0.55 \\
Patients with initial PEA/asystole & 199 (5) & 120 (4) & 0.14 \\
\hline
\end{tabular}
\end{table}
EMS Treatment of Cardiac Arrest

Data for cardiac arrest, attended but untreated by EMS, were available for Seattle. Women received ACLS or BLS less frequently than men (64% versus 69%, \(P<0.0001\)); in other words, women were attended but untreated more than men. Among those who received treatment, a higher proportion of men (87%) than women (82%) received ACLS as opposed to BLS (\(P<0.0001\)). However, after controlling for VF, the treatment rates were similar; the lower incidence of VF in women presumably contributed to their less frequent treatment.

Discussion

We examined an extensive database of out-of-hospital cardiac arrests in Seattle and suburban King County. Women were found in cardiac arrest half as often as men. However, women with cardiac arrest had significantly lower unadjusted survival rates than men. This was not surprising, because women had much lower rates of VF, were older, and had arrests that were less frequently witnessed and that occurred less frequently in public locations.

Previous studies have found that women’s survival rates are lower than men’s.\(^7\)\(^-\)\(^9\) In the various case studies, the reported unadjusted rates may reflect the higher proportions of men versus women with VF and the degree to which the outcomes for VF patients are improved compared with patients with other rhythms or asystole. After multivariate adjustment, the survival rates in men and women were similar. In our study, the primary reason for women’s lower survival seemed to be their lower rates of VF, a relatively favorable rhythm. Once we adjusted for VF, the difference in survival between men and women largely disappeared.

We observed that the lower rate of VF in women persisted after adjustment for age, witnessed arrest, bystander CPR, location of arrest, and EMS response times. There may be several reasons women have lower relative rates of VF than men. It is possible that women have a greater proportion of arrests due to noncardiac causes than men and that these arrests lead to PEA or asystole more often than VF. This is supported by the greater prevalence of cardiac causes among men in the suburban King County database, although not in the Seattle database. It is also possible that women have different causes for primary cardiac arrest than men and that these different causes predispose to PEA or asystole. In support of this explanation, autopsy studies of selected cardiac arrest patients have demonstrated different cardiac abnormalities in men and women. Specifically, the presence of hypertrophy was more frequent in men who died of cardiac arrest than in women.\(^16\) Additionally, a study of cardiac arrest survivors found that women were significantly less likely to have underlying coronary disease than men and were more likely to have other forms of heart disease or structurally normal hearts.\(^17\) The Framingham study also found that traditional coronary ischemia risk factors were stronger predictors of sudden cardiac death in men than in women.\(^2\)

Although it is possible that different rates of coronary disease in men and women contribute to the different rates of VF, the fact that VF rates did not vary across different age strata suggest that this is not the only reason. This is because the difference between coronary disease rates between men and women diminishes with age,\(^18\) whereas the VF difference is fairly consistent. It is unlikely that the lower rates of VF in women could be due to EMS factors, such as response intervals or CPR performance, because women had lower rates of VF even after adjustment for multiple factors. Therefore, the reasons for the lower relative rate of VF in women remain unclear.

After adjustment for VF, women were more likely to be resuscitated and admitted to the hospital than men. Among patients with VF, younger women had higher prehospital resuscitation than younger men. Such sex differences were greatest for patients between 30 and 39 years of age and decreased successively across older age groups. The reasons for this advantage and why it was lost during the course of hospital stay are unclear. Although a sex-age interaction has not been previously examined for cardiac arrest, it has been found in patients categorized as having myocardial ischemia. In these studies, younger women actually had higher mortality than younger men.\(^12\)\(^,\)\(^13\) The reasons for the interaction in ischemia patients are unclear; the literature references possible explanations such as ovarian dysfunction, deficiency of ovarian receptors, social isolation, and emotional stress in young women with ischemia. Plaque erosion may be associated with estrogen status, whereas traditional risk factors may be associated with plaque formation and morphology in women.\(^19\) Interestingly, the studies also hypothesize that a different threshold of hospital admission might increase the proportion of young women with severe ischemia admitted to the hospital, which would artificially increase hospital mortality in younger women with ischemia. This was based on the observation that the 28-day cardiac case-fatality rate in Scottish men and women was similar and that men had higher fatality rates out of hospital but that women had higher fatality rates once admitted.\(^11\) However, this assumes that patients have a fixed course of disease after cardiac arrest and that patients who survive prehospital will only die in-hospital.

It is possible that young women in VF cardiac arrest are affected by similar factors. Patients of lower socioeconomic status are less likely to survive out-of-hospital cardiac arrest due to VF, and young men may be more disadvantaged than young women in this regard.\(^20\) Also, the diseases that cause VF in younger women may be more responsive to prehospital treatments such as defibrillation and ACLS than diseases that cause VF in young men. As women and men age and coronary disease becomes more likely in both sexes, this response difference could be lost.

Alternatively, young women and men may have similar causes of VF, but perhaps the disease in young women is more responsive to defibrillation and ACLS. Specifically, sex hormones present in young women may figure in their greater resuscitation rates. For example, women may metabolize antiarrhythmic drugs differently than men at different points in their menstrual cycle, which could lead to different responses to treatment in younger women.\(^21\) Also, young women may be less likely to manifest cardiac arrhythmias at different points in their menstrual cycle.\(^22\)\(^,\)\(^23\) Women’s smaller size may lead to decreased electrical impedance and increase the success of cardioversion. Finally, after admission...
for cardiac arrest, it is also possible that men and women receive different treatment, which in turn affects their outcome, such as those differences in medication and procedure use sometimes documented for cardiac ischemia. Also, the database considers only cases for which EMS was summoned. It is unclear to what degree the cases represent all cases of out-of-hospital cardiac arrest, although we think that virtually all sudden deaths in the study area have EMS involvement. It is possible, however, that the rate of EMS use is lower for women than for men. We did not have hospital treatment data on all patients in our combined databases, so we could not assess the effect of comorbidity on responses to procedures and medications. Finally, we could not fully explore the role of cardiac cause due to the differing definitions between the Seattle and suburban King County databases; it is possible that cause could explain why young men and women were resuscitated at different rates and why they had different rates of VF. Exploration of the likelihood of certain diseases to result in VF versus other rhythms, along with closer examination of arrest in cause in a random selection of cardiac arrest patients, could provide insight into the different rates of VF in men and women.

Conclusions

The incidence of out-of-hospital cardiac arrest in women was about half that of men. When adjusted for the presence of VF, the overall EMS treatment rates for men and women were similar. Women had lower unadjusted resuscitation and survival rates compared with men, primarily because of their lower incidence of VF. After adjustment for VF and other baseline differences, women had a higher resuscitation rate and a similar survival rate compared with men. Young women in VF had a higher resuscitation rate than young men in VF, and this difference diminished with age. Future investigations should examine the causes of cardiac arrest in women to explore whether types of heart disease or hormonal fluctuation relate to the lower incidence of cardiac arrest, rates of VF, and outcomes of treatment. In particular, the influence of hormones on VF rates and response to treatments in younger women should be explored.

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References

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